Indication
ZOLGENSMA® (onasemnogene abeparvovec-xioi) is a prescription gene therapy used to treat children less than 2 years old with spinal muscular atrophy (SMA). ZOLGENSMA is given as a one-time infusion into a vein. ZOLGENSMA was not evaluated in patients with advanced SMA.

Important Safety Information
ZOLGENSMA can cause acute serious liver injury. Liver enzymes could become elevated and may reflect acute serious liver injury in children who receive ZOLGENSMA. Patients will receive an oral corticosteroid before and after infusion with ZOLGENSMA and will undergo regular blood tests to monitor liver function. Contact the patient’s doctor immediately if the patient’s skin and/or whites of the eyes appear yellowish, or if the patient misses a dose of the corticosteroid or vomits it up.

Please see additional Important Safety Information on page 17 and the accompanying Full Prescribing Information.

I’ll always remember the day we received the one-time-only dose for SMA

Malachi, treated at ~4 months and pictured at 4 years, was diagnosed with SMA Type 1.
ZOLGENSMA stops the progression of SMA with a one-time-only dose

This guide will help you learn more about ZOLGENSMA® (onasemnogene abeparvovec-xioi), a one-time infusion for the treatment of children less than 2 years old with spinal muscular atrophy (SMA).

Ask your doctor if ZOLGENSMA is the right choice for your child with SMA.

Evelyn, treated at ~2 months and pictured at 4½ years, was diagnosed with SMA Type 1.

Important Safety Information

Viral respiratory infections before or after ZOLGENSMA infusion can lead to more serious complications. Contact the patient’s doctor immediately if you see signs of a possible viral respiratory infection such as coughing, wheezing, sneezing, runny nose, sore throat, or fever.

Please see the Indication and additional Important Safety Information on page 17 and the accompanying Full Prescribing Information.
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### Important Safety Information

Decreased platelet counts could occur following infusion with ZOLGENSMA. Seek immediate medical attention if the patient experiences unexpected bleeding or bruising.

Please see the Indication and additional Important Safety Information on page 17 and the accompanying Full Prescribing Information.
What is spinal muscular atrophy (SMA)?

SMA is a progressive, rare genetic disease, yet it is the number one genetic cause of infant death.

About 1 in 50 people in the United States (or 6.6 million* Americans) is a genetic carrier of SMA, and most don’t know it.

A carrier is a person who has a mutation in 1 copy of a gene but doesn’t have the disease.

SMA affects about 1 in every 11,000 babies born each year.

*Calculations are based on an estimated US population of 330 million.

What causes SMA?

The genetic cause of SMA is a survival motor neuron 1 (SMN1) gene that is missing or not working properly. When this main gene is missing or not working properly, the body cannot make enough survival motor neuron (SMN) protein, which is needed for motor neuron cell survival. Everyone is born with a certain amount of motor neuron cells, which are responsible for communicating with the muscles and telling them to work properly.

Without enough SMN protein, motor neuron cells become weaker and weaker and eventually stop working, lose all function, and die. As a result, things many of us take for granted, like breathing, eating, speaking, and lifting the head, become difficult. Once motor neuron cells die, they cannot be brought back.

Learn more about the cause of SMA
The role of a backup gene

There is a backup gene for the SMN1 gene, called the SMN2 gene. People can have 1 or more copies of this backup gene. This gene, like the SMN1 gene, tells the body to make SMN protein. For people with SMA, the SMN2 gene is the main source of SMN protein production; however, it is unable to produce as much protein as the SMN1 gene. That is why it is essential to replace the function of the missing or nonworking SMN1 gene.

In fact, the SMN2 gene makes only about 10% of working SMN protein compared to the protein produced by the SMN1 gene. Even people with several copies of the SMN2 gene may not produce as much SMN protein as those with a working SMN1 gene, and their motor neuron cells may not work as they should. Usually, the more copies of the SMN2 gene a person has, the less severe his or her SMA is.
A mother’s powerful persistence

When Maisie was diagnosed with spinal muscular atrophy (SMA) Type 1, her mother, Ciji, knew she would need to become a powerful advocate for her daughter. From the beginning, Ciji wanted her daughter to be treated with ZOLGENSMA® (onasemnogene abeparvovec-xioi). However, when Maisie was diagnosed, ZOLGENSMA was not yet FDA-approved, and she didn't qualify for the clinical studies. Ciji understood that time is of the essence in SMA, so she started Maisie on an FDA-approved treatment when she was ~6 months old. Despite this, Ciji was still drawn to ZOLGENSMA as a treatment option because it targets the genetic root cause of SMA with one dose.

Her determination to advocate for her daughter prevailed when Maisie was treated with ZOLGENSMA at about 20 months old. At 2 years old, Maisie has achieved mobility milestones, but for Ciji, the greatest milestone will always be the first time Maisie said, “Momma.”

Important Safety Information

Thrombotic microangiopathy (TMA) has been reported to occur approximately one week after ZOLGENSMA infusion. Caregivers should seek immediate medical attention if the patient experiences any signs or symptoms of TMA, such as unexpected bruising or bleeding, seizures, or decreased urine output.

Please see the Indication and additional Important Safety Information on page 17 and the accompanying Full Prescribing Information.
The one-time-only dose for the treatment of SMA

With one dose, ZOLGENSMA® (onasemnogene abeparvovec-xioi) stops the progression of SMA. It is a gene therapy that is designed to replace the function of the missing or nonworking gene that causes SMA. ZOLGENSMA is not a cure and cannot reverse damage already caused by SMA before treatment.

How ZOLGENSMA is given

ZOLGENSMA is given as a one-time infusion into a vein over 60 minutes at a treatment center.

Important Safety Information

Talk with the patient's doctor to decide if adjustments to the vaccination schedule are needed to accommodate treatment with a corticosteroid. Protection against respiratory syncytial virus (RSV) is recommended.

Please see the Indication and additional Important Safety Information on page 17 and the accompanying Full Prescribing Information.
Targeting the genetic root cause of SMA

As a gene therapy, ZOLGENSMA® (onasemnogene abeparvovec-xioi) is designed to target the genetic root cause of SMA by replacing the function of the missing or nonworking SMN1 gene with a new, working copy of a human SMN gene. ZOLGENSMA does not change or become a part of a child's DNA. To help you understand how this is possible, let's look at how ZOLGENSMA works to treat SMA.

Important Safety Information

Temporarily, small amounts of ZOLGENSMA may be found in the patient's stool. Use good hand hygiene when coming into direct contact with bodily waste for 1 month after infusion with ZOLGENSMA. Disposable diapers should be sealed in disposable trash bags and thrown out with regular trash.

Please see the Indication and additional Important Safety Information on page 17 and the accompanying Full Prescribing Information.
With the motor neuron cells now able to make sufficient SMN protein, motor neuron cells that have not died may survive, function, and be maintained.

When the new gene reaches its destination, it is ready to tell the motor neuron cells to start making SMN protein. This happens throughout the body, delivering a new, working copy of the SMN gene to motor neuron cells. The new gene does not become part of the child’s DNA.

The vector that delivers the SMN gene is made from a virus called adeno-associated virus 9, or AAV9. This type of virus is not known to make people sick. To make the vector, the DNA of the virus is removed so that the new SMN gene can be put inside. Vectors are used because they can travel throughout the body and deliver the new, working gene to the cells where it is needed.

ZOLGENSMA® (onasemnogene abeparvovec-xioi) is made up of a new, working copy of a human SMN gene that is placed inside a vector. A vector’s job is to take the new, working SMN gene to the motor neuron cells in the body.

Important Safety Information
The most common side effects that occurred in patients treated with ZOLGENSMA were elevated liver enzymes and vomiting.

Please see the Indication and additional Important Safety Information on page 17 and the accompanying Full Prescribing Information.
The efficacy and safety of ZOLGENSMA® (onasemnogene abeparvovec-xioi) have been established in 3 clinical studies (2 completed and 1 ongoing) and 1 ongoing long-term follow-up study.

Two of the clinical studies enrolled patients who were treated after symptoms appeared (symptomatic) and 1 study enrolled patients who were treated before symptoms appeared (presymptomatic).

ZOLGENSMA was shown to stop the progression of SMA with a one-time-only dose given through an intravenous (IV) infusion over 60 minutes.

Important Safety Information

ZOLGENSMA can cause acute serious liver injury. Liver enzymes could become elevated and may reflect acute serious liver injury in children who receive ZOLGENSMA. Patients will receive an oral corticosteroid before and after infusion with ZOLGENSMA and will undergo regular blood tests to monitor liver function. Contact the patient's doctor immediately if the patient's skin and/or whites of the eyes appear yellowish, or if the patient misses a dose of the corticosteroid or vomits it up.

Please see the Indication and additional Important Safety Information on page 17 and the accompanying Full Prescribing Information.
STR1VE clinical study (completed)

The purpose of the STR1VE study was to evaluate the efficacy and safety of ZOLGENSMA® (onasemnogene abeparvovec-xioi).

The STR1VE study enrolled 22* symptomatic patients, which means they displayed symptoms of SMA before receiving treatment. All patients were diagnosed with SMA Type 1, had 2 copies of the SMN2 backup gene, and were 6 months of age or younger at the time of treatment.

- Average age at dosing was 3.7 months (0.5-5.9 months)
- Patients in the study were followed through their 18 months of age study visit
- Patients received the therapeutic dose of ZOLGENSMA (dose approved by the FDA)

*One patient was initially classified as presymptomatic but was later confirmed to be symptomatic and was included in the final clinical study findings.

Important Safety Information

Viral respiratory infections before or after ZOLGENSMA infusion can lead to more serious complications. Contact the patient's doctor immediately if you see signs of a possible viral respiratory infection such as coughing, wheezing, sneezing, runny nose, sore throat, or fever.

Please see the Indication and additional Important Safety Information on page 17 and the accompanying Full Prescribing Information.
STR1VE clinical study results

ZOLGENSMA increased event-free survival

At the 14 months of age study visit, 91% (20/22)* of patients were alive and did not need permanent breathing support.

In the natural history of SMA Type 1 (children who haven’t received treatment), about 25% of children were alive without permanent breathing support at 14 months of age.

- 1 patient passed away at 7.8 months of age from causes unrelated to treatment
- 1 patient withdrew from the study at 11.9 months of age and required permanent ventilation at 11 months of age prior to leaving the study

*One patient was initially not part of the data set but is included in the final data analysis.

What is an event?
Event was defined as death, the need for permanent ventilatory support (such as tracheostomy), or the need for respiratory assistance (not due to illness or surgery) for 16 hours or more a day for at least 14 days.

Important Safety Information
Decreased platelet counts could occur following infusion with ZOLGENSMA. Seek immediate medical attention if the patient experiences unexpected bleeding or bruising.

Please see the Indication and additional Important Safety Information on page 17 and the accompanying Full Prescribing Information.
STR1VE clinical study results

ZOLGENSMA helped patients achieve the ability to sit without support

59%
(13/22) of patients could sit without help for at least 30 seconds at the 18 months of age study visit (end of study).

64%
(14/22) of patients could sit without support for at least 30 seconds at any point in the study.*

*One patient achieved the milestone of sitting independently for 30 seconds or more at 16 months of age, but this milestone was not reconfirmed at the 18 months of age study visit.

In the natural history of SMA Type 1, patients were not able to sit independently.

See more results from this study

Important Safety Information

Thrombotic microangiopathy (TMA) has been reported to occur approximately one week after ZOLGENSMA infusion. Caregivers should seek immediate medical attention if the patient experiences any signs or symptoms of TMA, such as unexpected bruising or bleeding, seizures, or decreased urine output.

Please see the Indication and additional Important Safety Information on page 17 and the accompanying Full Prescribing Information.
Meet Olivia from the STR1VE clinical study

In the wake of a spinal muscular atrophy (SMA) diagnosis, families can be left searching for hope. For Kirsten and Cody, that hope came in the form of the STR1VE clinical study.

Six weeks after their daughter, Olivia, was born she was experiencing loss of reflexes and weakness in her legs. Once their pediatric neurologist confirmed a diagnosis of SMA Type 1, Olivia’s family jumped into research and found promising results from the START clinical study, which prompted them to learn more about gene therapy and how it works. Right away, they were interested in ZOLGENSMA® (onasemnogene abeparvovec-xioi) because it was a one-time dose that could address the genetic root cause of SMA. Olivia qualified for the STR1VE clinical study and received treatment with ZOLGENSMA when she was about 2½ months old.

Fast-forward to age 2, and Olivia is sitting up unassisted, eating by mouth, and breathing on her own. Her parents feel like the sky’s the limit for Olivia as she continues to get stronger.

Important Safety Information

Talk with the patient’s doctor to decide if adjustments to the vaccination schedule are needed to accommodate treatment with a corticosteroid. Protection against respiratory syncytial virus (RSV) is recommended.

Please see the Indication and additional Important Safety Information on page 17 and the accompanying Full Prescribing Information.
Additional clinical studies

**Symptomatic patients: START study (completed)**

This was the first study of ZOLGENSMA® (onasemogene abeparvovec-xioi).

**Participants:** 15 patients with SMA Type 1 (2 copies of SMN2 backup gene) who were 8 months of age or younger at the time of infusion. Patients in the study were split into 2 groups. Three patients in group 1 received a low dose of ZOLGENSMA and 12 patients in group 2 received a higher dose.

**Goal:** Evaluate safety and determine the appropriate dose of ZOLGENSMA.

**START LTFU (ongoing)**

In addition, there is the START long-term follow-up (START LTFU) study. This voluntary, ongoing 15-year long-term follow-up study monitors the long-term safety of ZOLGENSMA in 13/15 patients from the START study.

**Presymptomatic patients: SPR1NT study (ongoing)**

This study includes patients who did not have symptoms of SMA. These patients continue to be evaluated.

**Participants:** 29* patients with 2 or 3 copies of the SMN2 backup gene who were 6 weeks of age or younger at the time of infusion. The study is still ongoing.

**Goal:** Evaluate the efficacy and safety of ZOLGENSMA when given before symptoms appear.

*One additional patient had 4 copies of the SMN2 backup gene.

See the results of the ongoing SPR1NT study

**Important Safety Information**

Temporarily, small amounts of ZOLGENSMA may be found in the patient’s stool. Use good hand hygiene when coming into direct contact with bodily waste for 1 month after infusion with ZOLGENSMA. Disposable diapers should be sealed in disposable trash bags and thrown out with regular trash.

Please see the Indication and additional Important Safety Information on page 17 and the accompanying Full Prescribing Information.
ZOLGENSMA® (onasemnogene abeparvovec-xioi) has an established safety profile demonstrated in 3 clinical studies and 1 observational long-term follow-up study.

44 patients were treated with ZOLGENSMA and ranged in age from 0.3 to 7.9 months at the time of infusion.

The most common side effects (5% or more) of ZOLGENSMA experienced in the clinical studies were elevated liver enzymes and vomiting.

Reports of pyrexia (or fever) and thrombotic microangiopathy (TMA) were identified during postmarketing experience.

Important Safety Information

The most common side effects that occurred in patients treated with ZOLGENSMA were elevated liver enzymes and vomiting.

Please see the Indication and additional Important Safety Information on page 17 and the accompanying Full Prescribing Information.

Safety data update

As of December 2019, 100 patients have been treated with ZOLGENSMA intravenously (IV) in clinical studies.

- The most common side effects of ZOLGENSMA experienced in the clinical studies were elevated liver enzymes and vomiting

- Safety data continue to be collected
Indication and Important Safety Information

What is ZOLGENSMA?
ZOLGENSMA is a prescription gene therapy used to treat children less than 2 years old with spinal muscular atrophy (SMA). ZOLGENSMA is given as a one-time infusion into a vein. ZOLGENSMA was not evaluated in patients with advanced SMA.

What is the most important information I should know about ZOLGENSMA?
- ZOLGENSMA can cause acute serious liver injury. Liver enzymes could become elevated and may reflect acute serious liver injury in children who receive ZOLGENSMA.
- Patients will receive an oral corticosteroid before and after infusion with ZOLGENSMA and will undergo regular blood tests to monitor liver function.
- Contact the patient's doctor immediately if the patient’s skin and/or whites of the eyes appear yellowish, or if the patient misses a dose of the corticosteroid or vomits it up.

What should I watch for before and after infusion with ZOLGENSMA?
- Viral respiratory infections before or after ZOLGENSMA infusion can lead to more serious complications. Contact the patient’s doctor immediately if you see signs of a possible viral respiratory infection such as coughing, wheezing, sneezing, runny nose, sore throat, or fever.
- Decreased platelet counts could occur following infusion with ZOLGENSMA. Seek immediate medical attention if the patient experiences unexpected bleeding or bruising.
- Thrombotic microangiopathy (TMA) has been reported to occur approximately one week after ZOLGENSMA infusion. Caregivers should seek immediate medical attention if the patient experiences any signs or symptoms of TMA, such as unexpected bruising or bleeding, seizures, or decreased urine output.

What do I need to know about vaccinations and ZOLGENSMA?
- Talk with the patient’s doctor to decide if adjustments to the vaccination schedule are needed to accommodate treatment with a corticosteroid.
- Protection against respiratory syncytial virus (RSV) is recommended.

Do I need to take precautions with the patient’s bodily waste?
Temporarily, small amounts of ZOLGENSMA may be found in the patient’s stool. Use good hand hygiene when coming into direct contact with bodily waste for 1 month after infusion with ZOLGENSMA. Disposable diapers should be sealed in disposable trash bags and thrown out with regular trash.

What are the possible or likely side effects of ZOLGENSMA?
The most common side effects that occurred in patients treated with ZOLGENSMA were elevated liver enzymes and vomiting.

The safety information provided here is not comprehensive. Talk to the patient’s doctor about any side effects that bother the patient or that don’t go away.

You are encouraged to report suspected side effects by contacting the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch, or Novartis Gene Therapies, Inc. at 833-828-3947.

Please see the Full Prescribing Information.
Ask your doctor if ZOLGENSMA is right for your child

If you want to explore whether ZOLGENSMA® (onasemnogene abeparvovec-xioi) is right for your child, visit your child’s doctor to discuss the potential benefits and potential risks of treatment and if your child qualifies for ZOLGENSMA. Your doctor can address questions or concerns you may have. If you and your doctor decide to pursue treatment with ZOLGENSMA, check out the next steps on the following page.

Important Safety Information

ZOLGENSMA can cause acute serious liver injury. Liver enzymes could become elevated and may reflect acute serious liver injury in children who receive ZOLGENSMA. Patients will receive an oral corticosteroid before and after infusion with ZOLGENSMA and will undergo regular blood tests to monitor liver function. Contact the patient’s doctor immediately if the patient’s skin and/or whites of the eyes appear yellowish, or if the patient misses a dose of the corticosteroid or vomits it up.

Please see the Indication and additional Important Safety Information on page 17 and the accompanying Full Prescribing Information.
Starting ZOLGENSMA

Pretreatment testing to determine if your child qualifies for ZOLGENSMA
Read more about Step 1

Connect with the OneGene Program
Read more about Step 2

Prepare for treatment day
Read more about Step 3

Treatment day
Read more about Step 4

After treatment with ZOLGENSMA
Read more about Step 5

Watch a video about the steps to treatment

Watch a short video and learn about starting ZOLGENSMA, including lab tests that are needed, what happens on treatment day, and support and care after treatment.

Support from the OneGene Program

Knowing what to expect and what you can do now will help you and your child prepare for treatment with ZOLGENSMA® (onasemnogene abeparvovec-xioi). Providing support along the way is the OneGene Program™. This program is a dedicated resource brought to you by Novartis Gene Therapies and is specifically designed to help you and your family. Contact the OneGene Program at 855-441-GENE (4363), Monday-Friday (8 AM-8 PM ET), to learn more about the support available to you.

Important Safety Information

Viral respiratory infections before or after ZOLGENSMA infusion can lead to more serious complications. Contact the patient’s doctor immediately if you see signs of a possible viral respiratory infection such as coughing, wheezing, sneezing, runny nose, sore throat, or fever.

Please see the Indication and additional Important Safety Information on page 17 and the accompanying Full Prescribing Information.
A community comes together

A diagnosis of spinal muscular atrophy (SMA) can be overwhelming. Thankfully, Nicole and Tyler found support and expertise at every step of their journey to treatment.

Their son, Brady, was born in 2018. At around 9 months old, Nicole noticed Brady could not stand, even with assistance. She was referred to a pediatric neurologist who diagnosed Brady with SMA Type 2 in 2019 when he was about 13 months old. A genetic specialist explained the treatment options, and after learning about ZOLGENSMA® (onasemnogene abeparvovec-xioi) and that it was a one-time-only dose, they felt it was the best option for Brady.

From there, the pediatric neurologist, insurance company, OneGene Program™, and Patient Resource Manager (PRM) all worked together to help Brady receive treatment with ZOLGENSMA. Now at 2 years old, he is a bundle of energy and gives his parents a reason to celebrate each and every day!

Important Safety Information

Decreased platelet counts could occur following infusion with ZOLGENSMA. Seek immediate medical attention if the patient experiences unexpected bleeding or bruising.

Please see the Indication and additional Important Safety Information on page 17 and the accompanying Full Prescribing Information.
Additional resources to help you navigate life with SMA after treatment

Start the next chapter in your SMA journey with the help of SMA Atlas—a valuable online resource that provides information, guidance, and inspiration from caregivers about life with SMA after treatment. Some of the topics and stories you will discover include:

- How to build a healthcare team
- Tips on advocating for your child
- Family-fun activities
- Supportive therapies 101
- Caregiver memorable moments

Get started on your new SMA journey

Please see the Indication and Important Safety Information on page 17 and the accompanying Full Prescribing Information.
Talk to your doctor about ZOLGENSMA® (onasemnogene abeparvovec-xioi) and visit ZOLGENSMA.com to learn more.

Watch videos, download resources, and learn about connecting with the SMA community.

Please see the Indication and Important Safety Information on page 17 and the accompanying Full Prescribing Information.